Chapter 9

General discussion and future perspectives

General discussion

The goal of all fracture treatment is to achieve early return to function and mobility. Key principles in fracture treatment are 1) fracture reduction and fixation to restore anatomical relationships, 2) fracture fixation providing absolute or relative stability as the "personality" of the fracture, the patient, and the injury requires, 3) preservation of the blood supply to soft tissues and bone by gentle reduction techniques and careful handling, and 4) early and safe mobilization and rehabilitation of the injured part and the patient as a whole[1].

A femoral shaft fracture in adults is typically an injury of working age people[2]. The mean age in this group is around 40 years[3,4]. This injury may have considerable impact on a patient's physical, psychological and social functioning.

The general aim of this thesis was to evaluate outcome of unreamed nailing of acute traumatic femoral shaft fractures. Clinician - as well as patient - reported outcome measures are used in this study.

Since 1995, our standard of care for femoral shaft fractures in adult patients (except in critically injured polytraumatized patients) includes early total care using an unreamed nailing technique. Both antegrade and retrograde nailing techniques have been employed in the treatment of our patients.

Part one: doctor reported outcomes

One of the main questions in modern literature concerning the nailing technique used in the treatment of femoral shaft fractures is: to ream or not to ream the medullary canal. A major contribution in this discussion is the supposed positive influence of reaming in the prevention of occurrence of delayed or non-unions. In this thesis we describe the incidence of non-union following antegrade unreamed nailing of femoral shaft fractures (**chapter 3**) to be 1.9%. This low percentage is comparable to large series in which the femoral shaft was reamed[5,6].

Several randomized and quasi-randomized trials[7-11] have been published comparing reamed and unreamed antegrade nailing of femoral shaft fractures. Two systematic reviews as well have reported the effect of reaming[12,13]. Trials and both reviews showed that reamed intramedullary nailing has significantly lower non-union rates than unreamed intramedullary nailing. This is in line with other potential advantages like lower delayed union rates, and lower re-operation rates. There are other aspects that merit particular attention. The

aforementioned benefits must be traded off against an increased blood loss and longer operation times. A profound study of the literature showed no statistically significant differences between reamed and unreamed nailing when comparing rates of infections, pulmonary complications (adult respiratory distress syndrome), and mortality. Though the use of the unreamed nailing technique may be beneficial for some patient categories, such as polytraumatized patients in whom speed and minimizing blood loss are important, or those who preclude the administration of blood products (for example Jehovah's Witnesses). In this we take into consideration that treating polytrauma patients by fracture manipulation and nail insertion leads to secondary embolization of fat and bone marrow contents (reaming) from the fracture site which may result in secondary lung and brain injuries. Add to this the thought that a second hit (early surgery within days) preceded by the first hit (i.e. the traumatic event) may lead to a devastating inflammatory response, ultimately resulting in ARDS and MOF[14,15].

The quality of the literature on femoral shaft treatment does not provide sufficient evidence to favour a particular treatment. There are still insufficient well-conducted randomized controlled trials comparing reamed and unreamed nailing. The sample sizes of the published studies are limited and there may be a risk of bias among these studies. Available prospective and retrospective studies may be biased due to differences in patient selection, postoperative care that is provided, loss to follow-up, and incomplete outcome data. Inconsistent definitions of outcomes (such as non-union and delayed union) further make it difficult to interpret the results from various studies. Furthermore, study results may differ between patients with isolated femoral shaft fractures compared to polytrauma patients, particularly those with head or pulmonary injuries.

Based on our experience with non-reaming nailing techniques of femoral shaft fractures we consider the incidence of non-union to be low (1.9%)[11] and to be comparable with the best results of reamed nailing in the literature. Therefore we in general find no indication to ream the medullary canal in cases of traumatic femoral shaft fractures.

Retrograde nailing is an attractive alternative to antegrade nailing of femoral shaft fractures. Potential advantages include the ease of nail insertion and its applicability to polytrauma patients and those with multiple fractures needing multiple procedures during the initial surgical care[16,17].

Concerning fracture related items: cohort studies that compared antegrade and retrograde femoral nailing found no differences with respect to rates of union, malalignment, and reoperation[18-22]. However, there were serious inconsistencies in these studies regarding the time to achieve bone healing, ranging from 1.3 to 15 months. A review of the literature eventually showed a 96% union rate after retrograde femoral nailing compared to 98% after antegrade nailing[23]. We found in our series a union rate of 94% (95% CI: 88.1 – 97.2%) after retrograde unreamed nailing (**chapter 4**).

Retrograde nailing involves insertion of the nail through the knee and may result in knee problems, such as septic arthritis, knee function deficits and persistent knee pain.
Septic arthritis is a feared complication after retrograde nailing. Contamination of the knee is thought to occur either directly from the surgical entry or, in case of an open fracture, via communication from the open fracture site. In our case series, we found one patient (0.75%, 95% CI:0.04 – 4.7%) who (after two years) developed septic arthritis of the knee after retrograde nailing of a closed fracture (**chapter 4**). This low incidence is comparable to what Papadokostakis et al[23] found in their systematic review. They reported that the risk of a septic knee was 0.18% (0.03 – 1.0 %) after retrograde nailing of femoral fractures.
Retrograde nailing in open fractures introduces the risk of an infection at the fracture site to communicate with the knee joint. In literature concerning open fractures[24-26] it is suggested that the incidence of acute septic knee is low, ranging from 0% to 1.1%. We found no cases of septic arthritis in our series. The small sample sizes of our studies preclude a definitive conclusion regarding the risk of septic arthritis. Based on our experience and in view of the literature, retrograde nailing seems a safe and acceptable treatment, even in treating gunshot femur fractures[27-29]. This postulation is supported by Bible et al[30] who compared 34 retrograde to 24 antegrade nailing procedures in patients with ipsilateral traumatic knee arthrotomies. All patients required irrigation and debridement. There were no cases of septic arthritis in the retrograde nailing group.
Knee function deficits may occur after retrograde nailing. Though, knee flexion of at least 120 degrees was seen in the majority of our patients (**chapter 4 and 5**). Papadokostakis et al[23] showed that the mean range of motion of the knee in patients with femoral shaft fractures was 127.6 degrees when retrograde nailing was used. Comparative studies[8,19,21,22]

reported no differences in range of motion of the knee between antegrade and retrograde nailing of femoral shaft fractures.

Retrograde nailing is often associated with a higher incidence of knee pain than antegrade nailing. In a review of the literature, Katsoulis et al[31] found a mean incidence of knee pain after antegrade femoral nailing of 18.6% (range: 8.7 % - 37%) after a mean follow-up period of 18,3 months (ranging from 29.1 to 45.7 months). The mean incidence of knee pain after retrograde nailing was 25.6% (range: 1.1% - 55%) with a mean follow-up period of 15.9 months (ranging from 9 to 24 months). In another review, Brewster[32] found a large difference in the incidence of knee pain during follow-up : retrograde nailing produced knee pain during follow-up in 40-53% of the patients compared to 20% after antegrade nailing. Although at the end of follow-up this difference narrowed to 12.5% (antegrade nailing) and 23-24% (retrograde nailing) it suggests that patients who were treated with a retrograde nail are more likely to suffer chronic knee pain than patients who received an antegrade nail. In our study, persistent knee pain during follow-up was seen in 23% of our patients after retrograde nailing **(chapter 5).** An additional finding was that age was found to be the only independent predictor of patients reporting knee pain after retrograde femoral nailing. Possible explanations include higher physical demands in younger adults or higher pain tolerance in older patients.

The main cause of knee pain appeared to be hardware related[18,21,33-35]. A vast majority of patients suffering from knee pain after retrograde nailing symptoms became asymptomatic after removing the metal work. In our study (**chapter 5**), knee pain improved or disappeared in all symptomatic patients. It seems that long-term knee pain can be prevented by either removing the hardware or meticulous inserting the nail and the use of the correct length of the screws in the first place, especially in the condylar region.

Other sources of knee pain may be the result of concomitant ipsilateral soft tissue knee injuries (e.g. injuries of the ligaments and meniscus), reported in more than 50% of the patients[36-38]. Knee pain may also arise from degenerative changes secondary to an alteration in the mechanical axis of the femur after union[39,40]. Damage of the patellofemoral articulation after retrograde femoral nailing has been a persistent concern for those whom doubt about the appropriateness of the indication for retrograde nailing. However, various authors[16,41,42] who have used arthroscopy to remove the nail and found no evidence of patellofemoral articular lesions other than fibrous tissue. In our study, it seemed very

doubtful that knee pain is caused by any adverse effect on the patellofemoral articulation, because all complaints improved after removal of the nail. This finding in combination with the fact that the majority of the patients had an acceptable knee range of motion (≥ 120 degrees) makes the end result more than acceptable.

Part two: patient reported outcomes

Different outcome measurement instruments are used in trauma care. Traditional measures of outcome include rates of mortality and morbidity, physiological parameters such as radiographic evaluation of bone healing, and clinician-based measures of impairment such as range of motion. Unfortunately, these measures correlate poorly with the patient's view of the success or failure of health care. Patient-reported outcome measures (PROMs) are an important source of information in this context, and provide clinicians with information that is complementary to traditional measures. Patient-reported outcomes are outcomes reported directly by patients themselves and not interpreted by an observer, such as a physician[43]. A patient-reported outcome, like a physician-reported outcome, should measure the concept it is intended to measure, for example: the effect of a disease (e.g. a fracture) on health and functioning from the patient perspective.

The vast majority of trauma patients survive their injuries. (Serious) injuries often result in varying types of disability with numerous social and economic consequences. The leading conceptual model of disability is the World Health Organization's International Classification of Functioning, Disability and Health (ICF)[44]. In the ICF, problems with functioning are categorized in three interconnected areas: Impairments, Activity limitations and Participation restrictions. Disability refers to difficulties addressed in any or all three areas of functioning. Functional status is often regarded as a clinical outcome, addressing change in a patient's condition as a result of an intervention or to distinguish individual differences in respect to treatment. One of the most common assessment methods for measuring various aspects of functioning are patient-reported questionnaires.

In trauma and orthopaedic surgery, numerous patient-reported questionnaires are used for this purpose. Frequently used in both clinical practice and clinical research is the Short Musculoskeletal Function Assessment (SMFA) questionnaire. This questionnaire was developed by Swiontkowski et al[45] to study differences in the functional status of patients with a broad range of musculoskeletal disorders, including all types of injuries. The 46-item

SMFA questionnaire consists of two parts: the dysfunction index and the bother index. The dysfunction index comprises 34 items for the assessment of the patient's perception of the amount of difficulty they perceive when performing certain functions (25 items), and how often they have difficulties performing specific functions (9 items). The bother index consists of 12 items that allow patients to assess how much they are bothered by problems in various functional areas (e.g. sleep and rest, recreation, work, and family). All items are scored on a 5-item Likert scale, ranging from 1 (good function/not bothered) to 5 (poor function/extremely bothered).

The aim of a functional assessment tool, such as the SMFA, is to offer a standardized measure of the actual physical limitations of a patient. This instrument then can be used to measure the direct impact of functional limitation on individual patients, to measure patient's change over time, and to compare the patient with other patients who have comparable musculoskeletal disorders or injuries. The SMFA is one of the outcome measures recommended by the American Academy of Orthopaedic Surgeons[46]. We have successfully translated and culturally adapted the Dutch version (SMFA-NL). Factor analysis demonstrated four subscales of the SMFA-NL (**chapter 6**): *upper-extremity dysfunction* (6 items), *lower-extremity dysfunction* (12 items), *problems ADL* (activity daily living; 20 items), and *mental and emotional problems* (8 items). These newly identified subscales of the SMFA-NL as well as the original two indices showed good internal consistency. The SMFA-NL appears to be a valid and reliable questionnaire for the assessment of functional status of patients with musculoskeletal disorders. This patient-reported outcome questionnaire can be used to compare different patient groups as well as for cross-cultural comparisons.

The interpretability of a multi-item instrument such as the SMFA-NL may be challenging. Interpretability is the degree to which one can assign qualitative meaning to an instrument's quantitative score or change of score[47]. A proper interpretability of a score is a precondition to use an (multi-item) instrument in clinical practice. Various types of information can be used to interpret scores on questionnaires. An extensive description of the study population is needed in order to know for what category of patients the scores are interpreted. An examination of the distribution of scores in the study sample, in terms of mean and standard deviation, is important for a proper interpretation of scores over the scale of an instrument. Secondly, the distribution of scores is important as it affects the values of several measurement properties, such as construct validity, reliability parameters and

responsiveness. Norm values for a measurement instrument, generally scores in the general population, facilitate the interpretation of scores on the measurement instrument. These scores can be used as reference values. Scores of relevant subgroups of patients can be compared to these normative data. In **chapter 7**, age- and gender-specific reference data for the SMFA-NL were obtained for the general Dutch population. Significant differences in SMFA-NL scores were found between men and women and between different age groups. These findings emphasize the importance of presenting age- and gender-specific normative values of the SMFA-NL. These normative values provide an opportunity to compare the health status of patients with musculoskeletal injuries against their age- and gender-matched peers in the general Dutch population.

For a proper interpretation of a measurement instrument score, additional information is needed. Not every change on a measurement instrument is a real or true change. Small changes may be due to measurement error. Determining the smallest detectable change (SDC) and the minimally important change (MIC) in future studies will further facilitate the interpretation of change scores on the SMFA. The SDC is the smallest detectable change beyond the measurement error, i.e. a change that falls outside the measurement error of the health status measurement. The MIC is defined as the smallest change in score in the construct to be measured, which patients perceive as important. It is used to reflect individual change that is of clinical importance. To date, there are no existing criteria for the SMFA change scores that represent a minimally important change.

In **chapter 8**, we have used one generic and three disease-specific patient-reported outcome questionnaires to evaluate long-term functional outcome after intramedullary nailing of traumatic femoral shaft fractures. The visual analogue score (VAS; 0 – 10 cm) was used to determine pain in the lower limb. Only adult patients with a femoral shaft fracture but no other injuries to the lower limbs or pelvis were included. With an average time to follow-up of 7.8 years, we observed that the range of motion (ROM) of the hip and knee joint was comparable between the affected and unaffected leg, regardless the nailing technique. This suggests that the ROM of both hip and knee joint returns to normal over time. We found no significant differences in the 4 functional outcome questionnaires (SMFA-NL, Harris Hip Score (HHS), Western Ontario and McMaster University Osteoarthritis Index (WOMAC), and Lysholm knee score) between the antegrade and retrograde nailing groups. The mean VAS pain score was comparable between the groups as well.

Interestingly, even years after surgery 17% of the patients still reported moderate to severe pain (VAS>3). Pain in the lower limb remained an important predictor and source of disability after femoral shaft fractures, despite the fact that patients achieved good functional outcome scores as measured by SMFA-NL, HHS, WOMAC, and Lysholm knee score. More research is needed to investigate the source of pain after femoral shaft fractures.

Conclusions

Both antegrade and retrograde nailing seem to be safe options for stabilization of femoral shaft fractures. These techniques provide similar results with regard to union, malunion and reoperation rates. The risk of septic arthritis after retrograde nailing seems reasonably low, even in open fractures. However, retrograde nailing may lead to significantly more knee pain (often hardware related) whereas antegrade nailing is associated with significantly more hip and thigh pain. These differences, as well as technical differences (such as finding the correct entry point) should be taken into consideration when planning intramedullary nailing of femoral shaft fractures.

Physical function is impaired by musculoskeletal injuries (e.g. femoral shaft fractures), and can give rise to long term disabilities (e.g. ability to participate in usual work or recreational activities). PROMs aim to capture patients' perspectives of health. Most commonly they are self-completed questionnaires such as the SMFA. The SMFA-NL is a valid and reliable instrument to assess the functional status of patients with musculoskeletal disorders and injuries. This instrument can be used to evaluate the outcome after femoral shaft fractures, from a patient's perspective. More research is needed though to facilitate interpretation of the SMFA-NL (change) scores.

Future Perspectives

Statically locked, reamed antegrade nailing is generally considered the standard nailing technique in femoral shaft fractures. However, the management of femoral shaft fractures continues to evolve. Overall, the quality of the existing literature on treatment of femoral shaft fractures is still limited to provide definitive conclusions regarding treatment superiority. Although femoral nailing is associated with high union rates and low complication rates, it is not necessarily a straightforward procedure. Multiple decisions must

be made, e.g. patient position, the use of (skeletal) traction, and temporary use of external fixation in polytrauma patients.

Furthermore, the choice of the optimal entry point for placement of the nail is crucial since a wrongly chosen entry point may lead to intra- and postoperative complications. The most important advantages of alternative entry sites, intercondylar in retrograde nailing and more lateral in antegrade nailing, are the technical ease of identifying the entry portal and reduced time of the procedure, especially in obese patients and multiply injured patients. It is unlikely that the entry site of a particular nail would have a significant effect on bone healing. More important are the entry site-related complications. Additional studies comparing different entry sites in antegrade and retrograde nailing are needed to further study the impact and indications of these alternative entry points.

New nail designs and locking techniques in themselves contributed to the important progress in the use of intramedullary nailing techniques. The design of the nail transformed from a straight unlocked nail into a more anatomical nail which has a helical geometry mimicking the dimensions of the femoral canal. Such a nail can facilitate nail insertion through a lateral portal and nail removal along its own pathway like a corkscrew. Although these helical-shaped nails may be associated with less soft tissue damage and easier finding of the entry point, insertion inaccuracy can produce malalignment and iatrogenic fractures. Further studies are required to investigate the advantages of these helically shaped nails over conventional antegrade femoral nails.

An interesting development in locking techniques is the angle-stable fixation of the intramedullary nail. Mechanical stability becomes more challenging with fractures in osteoporotic bone and in fractures extending more distally. Recently, angle-stable interlocking screws have been introduced to improve the construct stability of nails. So far, there are only biomechanical (animal and cadaver) studies suggesting the potential benefits of such locking systems. Its clinical relevance must be proven yet.

The ideal timing and treatment modality of definitive fixation of femoral shaft fractures in patients with multiple injuries has been an area of interest for several decades now. Despite numerous studies, the evidence for the effect of timing of fracture fixation is still inconclusive. Available systematic reviews do not support a specific strategy in timing the nailing procedure for femoral shaft fractures in patients with multiple injuries, brain injury, or chest injury. The literature suggests that, even in these patient populations, the rate of

ARDS and mortality is low. Recent progress in critical care make comparisons and conclusions about mortality and ARDS from recent studies with those published a decade ago difficult. Furthermore, differences in definitions of multiple injuries, ARDS, and early treatment may confound the results. Perhaps the best treatment for patients with multiple injuries is to perform early definitive treatment as soon as adequate resuscitation has been accomplished. Damage control surgery (DCS) should not be used as an excuse to place external fixations in every patient with multiple injuries. Timely definitive treatment is important. Further studies should define end points of adequate resuscitation and evaluate protocols for definitive fixation based on these end points.

Although it is clear that interlocking intramedullary nailing of femoral shaft fractures is the standard of care, debate still exists regarding some technical aspects of the procedure. One of them is the role of medullary reaming. Although the understanding of the local and systemic effects of reaming deepens, there will remain controversies in intramedullary reaming, particularly in certain subgroups of patients. Randomized trials with sound methodology should be conducted to evaluate: reamed versus unreamed intramedullary nailing, different types of nails and different techniques for nail insertion. The quality of such studies could and should be enhanced by a sufficient sample size based on outcomes-specific power calculations, uniformity in the recruitment of patients with a sufficiently long and complete follow-up, as much as possible blinding of patients, clinicians, and outcome assessors, adherence to the intention to treat principles, and the use of standard, validated outcome measures, including patient-reported outcome measures. In addition, studies of prognosis and rehabilitation are lacking. Patients may experience residual functional deficits following intramedullary nailing of femoral shaft fractures. Reduced muscle strength, pain and altered gait pattern have been demonstrated. These impairments could limit the patient's ability to return to pre-injury levels of functioning. It is necessary to develop and implement rehabilitation guidelines, targeted at impairments recognized after stabilization of femoral shaft fractures, to improve patient outcome.

In conclusion, even with the increasing evidence, there is still much research needed to find more accurate answers to our questions regarding the intramedullary nailing of trauma patients with a femoral shaft fracture.

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